DETAILED ACTION

Election/Restrictions

Claims 1-8 are currently pending in the application.

Applicant's election of group I and election of compound 17 with traverse to various species in the replies filed on 11/17/08 and 01/27/09 is acknowledged. The traversal is on the ground(s) that the claims relate to a single general inventive concept. This is not found persuasive because the claims recited in the instant application recite various groups which lack special technical features in view of Herbert who teaches compound 25 (as taught by applicant), well known in the art, and therefore render the invention not related to a single general inventive concept and consequently resulting in a lack of unity of invention. Moreover, given that the compounds of formula I, II, and III possess various functional groups that are different chemically and physically, the Examiner contends that such compounds do not relate to a single general inventive concept. However, upon further consideration, the Examiner has decided to withdraw the species election requirement and has opened examination to compounds that replace or enhance the function of SMN to alleviate or reduce phenotype of cells with low SMN protein levels.

Thus, the requirement is still deemed proper and is therefore made FINAL.

Claims 4-8 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected group and species, there being no allowable generic or linking claim. Claims 1-3 are examined on the merits herein.

Examiner also acknowledges that the method of treating a neurodegenerative disease or disorder with low SMN protein levels comprising administered compounds of formula I, II, and III appear to be free of the art.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 2-3 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention (**see M.P.E.P 608.01 (k)**).

Claims 2-3 are particularly vague and indefinite given that applicant is claiming a compound that comprises formula I, II, or III. Given that a compound is a single entity in and of itself, the Examiner asserts that a compound cannot contain another compound. As a result, one of ordinary skill in the art would not be able to fully ascertain the metes and bounds of the aforementioned claims.

As a result of the above inconsistencies, the aforementioned claims are unable to be examined as disclosed given that the scope of the claimed subject matter would not be able to be determined by one of ordinary skill in the art.

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Claims 2-3 are particularly vague and indefinite given that applicant is claiming compounds 1-39 comprising formula I, II, and III and yet applicant does not disclose the particular structures of the compounds or the formulas in the aforementioned claims. Thus, given that applicant did not particularly point out the structures of compounds 1-40 and what compounds are encompassed by formula I, II, and III in the invention, one of ordinary skill in the art would not be able to fully ascertain the metes and bounds of the aforementioned claims.

As a result of the above inconsistencies, the aforementioned claims are unable to be examined as disclosed given that the scope of the claimed subject matter would not be able to be determined by one of ordinary skill in the art.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for certain compounds of formula I, II, and III for the treatment of spinal muscular atrophy (SMA), does not reasonably provide enablement for every single compounds that replaces or enhances the function of SMN or for the treatment of all neurodegenerative diseases or disorders with low SMN protein levels. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The instant claims are drawn to a method of treating a neurodegenerative disease or disorder with low SMN protein levels comprising administering an effective amount of a compound that replaces or enhances the function of SMN to alleviate or reduce a phenotype of cells with low SMN protein levels. The instant specification fails to provide information that would allow the skilled artisan to practice the treatment of all neurodegenerative diseases or disorders with low SMN protein levels or to use all compounds that replace or enhance the function of SMN to alleviate or reduce a phenotype of cells with low SMN protein levels.

In re Sichert, 196 USPQ 209 (CCPA 1977)

To be enabling, the specification of the patent must teach those skilled in the art how to make and use the full scope of the claimed invention without undue experimentation. In re Wright, 999 F.2d 1557, 1561 (Fed. Cir. 1993).

Explaining what is meant by "undue experimentation," the Federal Circuit has stated:

> The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed to enable the determination of how to practice a desired embodiment of the claimed invention. PPG v. Guardian, 75 F.3d 1558, 1564 (Fed. Cir. 1996).[1]

The factors that may be considered in determining whether a disclosure would require undue experimentation are set forth by In re Wands, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing Ex parte Forman, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

1) the quantity of experimentation necessary,
2) the amount of direction or guidance provided,
3) the presence or absence of working examples,
4) the nature of the invention,
5) the state of the prior art,
6) the relative skill of those in the art,
7) the predictability of the art, and
8) the breadth of the claims.

These factors are always applied against the background understanding that scope of enablement varies inversely with the degree of unpredictability involved. In re Fisher, 57 CCPA 1099, 1108, 427 F.2d 833, 839, 166 USPQ 18, 24 (1970). Keeping that in mind, the Wands factors are relevant to the instant fact situation for the following reasons:

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[1] As pointed out by the court in In re Angstadt, 537 F.2d 498 at 504 (CCPA 1976), the key word is "undue", not "experimentation".

1. The nature of the invention, state and predictability of the art, and relative skill level

The invention relates to a method of treating a neurodegenerative disease or disorder with low SMN protein levels comprising administering an effective amount of a compound that replaces or enhances the function of SMN to alleviate or reduce a phenotype of cells with low SMN protein levels. The relative skill of those in the art is high, that of an MD or PHD. That factor is outweighed, however, by the unpredictable nature of the art. As illustrative of the state of the art, the examiner cites Chang et al. who teach the use of sodium butyrate (i.e. a compound that enhances the function of SMN to alleviate or reduce the low SMN protein level phenotype of motor neuron cells)in the treatment of spinal muscular atrophy wherein treatment of SMA-like mice resulted in increased expression of SMN protein in motor neurons of the spinal cord and resulted in significant improvement of SMA clinical symptoms (see abstract). Moreover, Chang et al. teach that mutation of the SMN genes are correlated with the development of SMA, but not every neurodegenerative disease with low SMN protein levels (see pg. 9808, left col., second paragraph).

2. The breadth of the claims

The claims are thus very broad insofar as they recite the “treatment of all neurodegenerative diseases with low SMN protein levels” and using “all

compounds that replace or enhance the function of SMN" in the aforementioned method of treatment. While the prior art and applicant discloses SMA as one type of such neurodegenerative disease, nowhere in the prior art is it disclosed that treatment with such compounds is therapeutically effective against other neurodegenerative diseases with low SMN protein levels. Moreover, applicant's own specification does not teach the use of every single possible compounds or compounds that do not fall under formulas I, II, and III that replace or enhance the function of SMN" in the treatment of SMA or any other neurodegenerative disease with low SMN protein levels. Consequently, one skilled in the art would not be able to use the full scope of the claimed invention without undue experimentation.

3. The amount of direction or guidance provided and the presence or absence of working examples

The specification provides no direction or guidance for the use of all possible compounds that replace or enhance the function of SMN nor for the treatment of all neurodegenerative diseases with low SMN protein levels. No reasonably specific guidance is provided concerning useful therapeutic protocols for all of the claimed compounds that replace or enhance the function of SMN, other than the compounds of table 1. The latter is corroborated by the working example on page 17.

The instant disclosure provides no evidence to suggest that this unique

activity of compounds of formula I, II, III or any other compound that enhances or replaces the function of SMN can be extrapolated to all neurodegenerative diseases or disorders with low SMN protein levels, and thus does not meet the "how to use" prong of 35 USC 112, first paragraph with regard thereto.

4. The quantity of experimentation necessary

Because of the known unpredictability of the art, and in the absence of experimental evidence, no one skilled in the art would accept the assertion that all compounds that replace or enhance the function of SMN could be predictably used for the treatments of every single neurodegenerative disease or disorder with low SMN protein levels as inferred by the claims and contemplated by the specification especially given the complexity of neurodegenerative disorders. Accordingly, the instant claims do not comply with the enablement requirement of §112, since to practice the invention claimed in the patent a person of ordinary skill in the art would have to engage in undue experimentation, with no assurance of success.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Chang et al. (PNAS, 2001, Vol. 98, No. 17, pgs. 9808-9813).

Chang et al. teach that proximal spinal muscular atrophy (SMA) is a disease characterized by degeneration of anterior horn cells of the spinal cord leading to muscular paralysis with muscular atrophy (see pg. 9808, left col. top paragraph). Chang et al. further teach that survival motor neuron genes (SMN1 and SMN2 genes) are typically present but loss of function mutation of both copies of SMN1 is correlated with the development of SMA (see pg. 9808, left col., top paragraph). Importantly, Chang et al. teach that SMN2 appears to modify disease severity in a dose-dependent manner as SMN protein levels are correlated with disease severity (see pg. 9808, left col., paragraph 2). Additionally, Chang et al. teach that mouse SMA models that genotypically and phenotypically mimic human SMA exist wherein the severity of the disease is correlated with the amount of intact SMN protein (see pg. 9808, right col. paragraph 2). While SMN1 gene tends to be affected by SMA, SMN2 copies tend to be intact (see pg. 9808, right col., paragraph 2). Thus, Chang et al. suggest that drugs that modify the pattern of SMN2 transcript in SMA patients to increase full length SMN mRNA expression and thus the amount of SMN protein may have a therapeutic effect for SMA patients (see pg. 9808, right col., paragraph 2). Of interest, Chang et al. demonstrated that oral administration of

sodium butyrate to intercrosses of heterozygous pregnant knockout transgenic SMA-like mice decreased the birth rate of severe types of SMA-like mice, and SMA symptoms were ameliorated for all three types of SMA-like mice (see abstract, pg. 9811 and 9812, left col, and table 1). Thus, these results suggest that sodium butyrate may be an effective drug for the treatment of human SMA patients (see abstract and pg. 9813, left col, paragraph 2).

Accordingly, the teachings of Chang et al. anticipate claim 1.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Samira Jean-Louis whose telephone number is 571-270-3503. The examiner can normally be reached on 7:30-6 PM EST M-Th. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/S. J. L./

Examiner, Art Unit 1617

04/01/2009

/SREENI PADMANABHAN/

Supervisory Patent Examiner, Art Unit 1617